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1: J Neurotrauma. 1999 Jul;16(7):603-15. Related Articles, Links

# Neuropathologic characterization of a rodent model of closed head injury--addition of clinically relevant secondary insults does not significantly potentiate brain damage.

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We have characterized the early brain pathology in Sprague-Dawley rats subjected to a modified Richmond impact acceleration model of closed head injury (CHI). This model was modified to produce maximal traumatic brain injury (TBI) in the absence of skull fracture, extracerebral or intracerebral hemorrhage, or brain contusion. We then used this model to assess the neuropathologic effects of superimposed secondary insults, which were designed to reflect a clinically relevant combination of hypotension and pyrexia. Acute neuronal injury, blood-brain barrier (BBB) integrity, axonal injury (AI), and glial activation were studied 4 1/2 hours following either CHI (group A), CHI plus secondary insults (group B), secondary insults alone (group C), or sham control injury (group D). There was evidence of limited AI following CHI in the lower medulla and upper cervical cord region, which was not modified by addition of secondary insult. Loss of dendritic microtubule-associated protein MAP2 immunoreactivity proved a reliable marker of acute neuronal damage, which was confined to subimpact and inferolateral cortical locations following CHI and was widespread after secondary insult. The pattern of plasma protein extravasation paralleled that of acute neuronal injury. We found no evidence of microglial activation, either local or generalized, by 4 1/2 hours. However, by this time CHI and secondary insults had combined to produce evidence of subimpact astrocyte activation, which was not apparent with either insult or injury alone. We conclude that in this modified Richmond model of CHI, when combined with secondary insults, there is no convincing potentiation of brain damage with the minor exception of astrocyte activation.

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1: J Neurotrauma. 1999 May;16(5):357-64. 

# Site-specific cleavage of 28S rRNA as a marker of traumatic brain injury.

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A cleavage product of 28S rRNA was isolated from ipsilateral hippocampus of rat brain subjected to lateral fluid percussion induced traumatic brain injury (TBI). Northern blot analysis demonstrated that the corresponding cDNA fragment hybridized to 28S rRNA and three cleavage products. Two of the cleaved rRNA fragments (1.3 kb and 0.9 kb) were also observed in differentiated PC12 cells undergoing apoptosis induced by NGF withdrawal. The third fragment (0.6 kb) was detected only in rat brain tissue subjected to trauma, suggesting specific cleavage of 28S following TBI. The 0.6-kb fragment was found only in cortex and hippocampus ipsilateral to the trauma site, but not in brain stem, contralateral cortex or contralateral hippocampus. 28S rRNA cleavage was detected beginning 2 h after trauma and reflected injury severity. Although cleavage of 28S rRNA has been reported in association with apoptosis in white blood cells and apoptosis occurs in the experimental head injury model used, the pattern of 28S rRNA cleavage observed with TBI differs from those observed in apoptotic PC12 cells or those reported for white blood cells. Thus, whereas 28S rRNA fragmentation appears to be a marker of posttraumatic brain injury, its precise role in the secondary injury process remains to be established.

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# Posttraumatic hypothermia in the treatment of axonal damage in an animal model of traumatic axonal injury.

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OBJECT: Many investigators have demonstrated the protective effects of hypothermia following traumatic brain injury (TBI) in both animals and humans. Typically, this protection has been evaluated in relation to the preservation of neurons and/or the blunting of behavioral abnormalities. However, little consideration has been given to any potential protection afforded in regard to TBI-induced axonal injury, a feature of human TBI. In this study, the authors evaluated the protective effects of hypothermia on axonal injury after TBI in rats. METHODS: Male Sprague-Dawley rats weighing 380 to 400 g were subjected to experimental TBI induced by an impact-acceleration device. These rats were subjected to hypothermia either before or after injury, with their temporalis muscle and rectal temperatures maintained at 32 degrees C for 1 hour. After this 1-hour period of hypothermia, rewarming to normothermic levels was accomplished over a 90-minute period. Twenty-four hours later, the animals were killed and semiserial sagittal sections of the brain were reacted for visualization of the amyloid precursor protein (APP), a marker of axonal injury. The density of APP-marked damaged axons within the corticospinal tract at the pontomedullary junction was calculated for each animal. In all hypothermic animals, a significant reduction in APP-marked damaged axonal density was found. In animals treated with preinjury, immediate postinjury, and delayed hypothermia, the density of damaged axons was dramatically reduced in comparison with the untreated controls ($p < 0.05$). CONCLUSION: The authors infer from these findings that early as well as delayed posttraumatic hypothermia results in substantial protection in TBI, at least in terms of the injured axons.

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